THERMODYNAMIC STABILITIES OF METAL COMPLEXES OF THE BIOLOGICALLY ACTIVE COMPLEXING AGENT, 2-ACETYLPYRIDINE SEMICARBAZONE (2-APS)

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ABSTRACT

The stability constants of the chelates formed by 2-acetylpyridine semicarbazone with $UO_2(II)$, Cu(II), Ni(II), Pb(II), Co(II), Zn(II) and Cd(II) have been determined pH-metrically in 75% (v/v) aqueous dioxan at various temperatures. The method of Bjerrum and Calvin [M. Calvin and K.W. Wilson, J. Am. Chem. Soc., 67 (1945) 2003; J. Bjerrum, Metal Ammine Formation in Aqueous Solution, Haase, Copenhagen, 1941] as modified by Irving and Rossotti [H.M. Irving and H.S. Rossotti, J. Chem. Soc., (1954) 2904] has been used to determine the $\bar{n}$ and pL values. The stability constants β have been computed on a VAX-11/750 computer using the weighted least-squares method patterned after that of Sullivan et al. [J.C. Sullivan, J. Rydberg and W.F. Miller, Acta Chem. Scand. 13 (1959) 2023]. The thermodynamic functions ΔG, ΔH and ΔS have also been calculated.

INTRODUCTION

Semicarbazones act as complexing agents for various metal ions. They have many analytical applications and they also play a significant role in various biological systems. From the analytical point of view, these are very good chelating agents for metal ions, since they produce highly coloured complexes. In the planning and selection of a chelate process for a specific purpose, knowledge of the stability constants is of utmost importance. Semicarbazones have significant antimicrobial activities. The activity of semicarbazones is due to their ability to chelate with traces of metal ions present in biological systems.

EXPERIMENTAL

See refs. 1–4 for the basic methods used in this paper. 2-Acetylpyridine semicarbazone (2-APS) was prepared [5] by reacting the requisite amounts

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of semicarbazide hydrochloride (Fluka A.R.) dissolved in equimolar amounts of ethanol and 2-acetyl pyridine (Fluka A.R.). The reaction mixture was boiled under reflux for 6–8 h on a water bath and then cooled overnight in a freezer. The white solid was recovered by filtration and recrystallised from ethanol. The purity of the compound was checked by elemental analysis, m.p., TLC, NMR, IR and UV. Its solution was prepared in dioxan. Me_4NOH (TMAH) (E. Merck A.G., Darmstadt) in 75% dioxan was used as titrant. $HClO_4$ was standardised and diluted to the required molarity (0.1 M) with conductivity water. $NaClO_4$ was used to maintain the ionic strength constant.

Dioxan was purified by refluxing it over sodium metal for several days.

The solutions of metal ions, viz. $UO_2(II)$, Cu(II), Ni(II), Pb(II), Co(II), Zn(II) and Cd(II) were prepared and standardised by conventional methods.

A digital pH meter ECIL, model pH 5651 in conjunction with a glass electrode was used for pH measurements. The pH meter was standardised with potassium hydrogen phthalate and phosphate buffers before the titration.

All measurements were made at a definite temperature maintained constant by using an MLW (West Germany, NBE type) thermostat. A VAX-11/750 computer was used for most of the calculation.

Titration technique

Investigations were carried out at four different temperatures, viz. 25 ± 0.5, 35 ± 0.5, 40 ± 0.5 and $50 \pm 0.5°C$ at an ionic strength of 0.1 M. For each set of experiments, the final volume was made up to 20 ml maintaining the 75% aqueous dioxan medium: (i) 2.0 ml $HClO_4$ (0.1 M) + 1.0 ml $NaClO_4$ (2.0 M) + 15 ml dioxan + 2.0 ml water; (ii) 2.0 ml $HClO_4$ (0.1 M) + 1.0 ml $NaClO_4$ (2.0 M) + 10.0 ml ligand (0.01 M) in dioxan + 5.0 ml dioxan + 2.0 ml water; (iii) 2.0 ml $HClO_4$ (0.01 M) + 1.0 ml $NaClO_4$ (2.0 M) + 10.0 ml ligand (0.01 M) in dioxan + 0.5 ml metal (0.02 M) + 5.0 ml dioxan + 1.5 ml water. During complexation the acidic proton in the ligand is replaced by an equivalent amount of metal(II).

From the titration curves of the above sets of solutions, the values of $\bar{n}$ and pL values were calculated. The corresponding values of stability constants were then computed using the weighted least-squares method of Sullivan et al. [4]. The weighted least-squares treatment determines that set of B_n values which makes the function

$$U \left[U = \sum_{n=0}^{N} (y - x - nx)\beta_n x^n \right]$$

nearest to zero, by minimising

$$S \left[S = \sum_{i=1}^{I} U^2(x_i y_i z_i) \right]$$

TABLE 1

Stability constants of bivalent metal complexes 2-APS at $\mu = 0.1$ M $NaClO_4$ and at different temperatures

	$UO_2(II)$	Cu(II)	Ni(II)	Pb(II)	Co(II)	Zn(II)	Cd(II)
(Temp. $50 \pm 0.5\,^{\circ}$C, p$K_1 = 5.00$)							
log K_1	3.74	3.65	3.49	3.35	3.21	3.19	3.02
log K_2	3.51	3.36	3.28	3.19	3.14	3.00	2.80
log β_2	7.25	7.01	6.77	6.54	6.35	6.19	5.82
S_{min}	0.1763	0.1521	0.1265	0.1052	0.1342	0.0859	0.1129
(Temp. $= 40 \pm 0.5\,^{\circ}$C, p$K_1 = 5.25$)							
log K_1	3.72	3.70	3.68	3.49	3.31	3.23	2.98
log K_2	3.51	3.38	3.46	3.13	3.12	3.02	2.87
log β_2	7.23	7.08	7.14	6.62	6.43	6.25	5.85
S_{min}	0.1346	0.1532	0.1785	0.1236	0.1452	0.1082	0.0896
(Temp. $= 35 \pm 0.5\,^{\circ}$C, p$K_1 = 5.46$)							
log K_1	3.87	3.76	3.65	3.50	3.46	3.25	3.16
log K_2	3.66	3.48	3.33	3.27	2.85	2.72	2.67
log β_2	7.53	7.24	6.98	6.77	6.31	6.07	5.83
S_{min}	0.1459	0.1672	0.1821	0.1596	0.1125	0.0759	0.0876
(Temp. $= 25 \pm 0.5\,^{\circ}$C, p$K_1 = 5.60$)							
log K_1	4.23	4.12	3.93	3.84	3.78	3.60	3.48
log K_2	4.00	3.89	3.71	3.31	3.52	3.20	3.02
log β_2	8.23	8.01	7.64	7.15	7.30	6.80	6.50
S_{min}	0.1236	0.1492	0.1640	0.1126	0.1349	0.0460	0.1086

with respect to the variation in β_n. We have reported the S_{min} values for different metal complexes. S_{min} has the same statistical distribution as χ^2 with K degrees of freedom and with weights defined in accordance with Sullivan et al. [4]. S_{min} can be equated to χ^2. The stability constants thus calculated are given in Table 1.

RESULTS AND DISCUSSION

For calculation of values of $\bar{n}$ and pL, a total volume of 19.67 instead of 20 ml, due to the volume contraction in the dioxan–water medium, has been taken. The values of $\bar{n}_H$ were calculated at various pH values from the titration curves. The value of pK_1 for the ligand was obtained by plotting $\log(\bar{n}_H/1 - \bar{n}_H)$ vs. pH ($\mu = 0.1$ M $NaClO_4$), and the values thus obtained were 5.0, 5.25, 5.46 and 5.60 at 50 ± 0.5, 40 ± 0.5, 35 ± 0.5 and $25 \pm 0.5\,^{\circ}$C, respectively. The regularity of the stability sequence can be correlated with a monotonic decrease in the ionic radii and monotonic increase in the second ionisation potential, which in passing from Cd(II) to $UO_2(II)$ may be taken

to indicate either that coordination has not altered the electronic ground state of the metal ions or that any modifications that have taken place are of secondary importance. For these chelates, values of $\bar{n}$ greater than 2.0 have not been obtained; it is therefore concluded that not more than two chelates i.e. $1:1$ and $1:2$ $(M:L)$ are formed in each system. The concentration of the metal ion used (0.0005 M) is very low; therefore, the formation of poly-nuclear complexes is negligible. The order of stability constants of the metal complexes of 2-acetylpyridine semicarbazone is $UO_2(II) > Cu(II) > Ni(II) > Pb(II) > Co(II) > Zn(II) > Cd(II)$. This order is in good agreement with the order found by Mellor and Maley [6] and Irving and Williams [7,8]. In all cases it was observed that the value of log $K_1 >$ log K_2.

The values of stability constants given in Table 1 reveal that stability constants decrease with increase in temperature along with pK values of the ligand. These results are in good agreement with those of Pitzer [9]. The thermodynamic parameters $(\Delta G,\ \Delta H$ and $\Delta S)$ have also been calculated by using the following relationships

$$\Delta G = -RT \ln K$$

$$\text{d} \log K/\text{d}(1/T) = \Delta H/2.303R$$

$$\Delta S = (\Delta H - \Delta G)/T$$

The overall free energy change, standard enthalpy and standard entropy changes at $25 \pm 0.5°$C are reported in Table 2. The negative free energy change (ΔG) becomes more negative with decrease in temperature suggest-ing an increase in the extent of complex formation at lower temperatures. The enthalpy changes are exothermic. The change in entropy upon com-plexation is also favourable for complexation.

Thus we conclude that the biologically active ligand 2-APS forms stable complexes at lower temperatures and the values are in the range 2.5–4.5 (for both log K_1 and log K_2). Even the transition elements show less tendency towards complexation with 2-APS.

TABLE 2

Thermodynamic functions for the formation of the bivalent metal complexes of 2-APS at $\mu = 0.1$ M $NaClO_4$ and temp. $= 25 \pm 0.5°$C

Metal ions	$-\Delta G$ (kcal mol^{-1})	$-\Delta H$ (kcal mol^{-1})	ΔS (kcal K^{-1} mol^{-1})
Cd(II)	4.745	4.113	0.0021
Zn(II)	4.868	3.199	0.0056
Co(II)	4.977	4.570	0.0003
Pb(II)	5.141	5.027	0.0003
Ni(II)	5.331	4.113	0.0040
Cu(II)	5.536	5.484	0.0001
$UO_2(II)$	5.645	4.570	0.0036

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